Original Article

A Novel Scoring System To Distinguish Vocal Cord Dysfunction from Asthma

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What is already known about this topic? Distinguishing vocal cord dysfunction from asthma can be difficult. Laryngoscopy remains the current criterion standard for the diagnosis of vocal cord dysfunction, although it is not available to all practitioners. Currently, there is no clinical scoring system to help distinguish the 2 disorders.

What does this article add to our knowledge? We developed a useful clinical scoring system to help distinguish vocal cord dysfunction from asthma.

How does this study impact current management guidelines? The Pittsburgh Vocal Cord Dysfunction Index may be a useful clinical tool to help prevent the misdiagnosis and mistreatment of vocal cord dysfunction as asthma.

BACKGROUND: Vocal cord dysfunction is often misdiagnosed and mistreated as asthma, which can lead to increased and unnecessary medication use and increased health care utilization.
OBJECTIVE: To develop a valid scoring index that could help distinguish vocal cord dysfunction from asthma.
METHODS: We compared the demographics, comorbidities, clinical symptoms, and symptom triggers of subjects with vocal cord dysfunction (n = 89) and those with asthma (n = 59). By using multivariable logistic regression, we identified distinguishing features associated with vocal cord dysfunction, which were weighted and used to generate a novel score. The scoring index also was tested in an independent sample with documented vocal cord dysfunction (n = 72).
RESULTS: We identified symptoms of throat tightness and dysphonia, the absence of wheezing, and the presence of odors as a symptom trigger as key features of vocal cord dysfunction that distinguish it from asthma. We developed a weighted index based on these characteristics, the Pittsburgh Vocal Cord Dysfunction Index. By using a cutoff of ≥4, this index had good sensitivity (0.83) and specificity (0.95) for the diagnosis of vocal cord dysfunction. The scoring index also performed reasonably well in the independent convenience sample with laryngoscopy-proven vocal cord dysfunction and accurately made the diagnosis in 77.8% of subjects.
CONCLUSION: The Pittsburgh Vocal Cord Dysfunction Index is proposed as a simple, valid, and easy-to-use tool for diagnosing vocal cord dysfunction. If confirmed by a prospective evaluation in broader use, it may have significant clinical utility by facilitating a timely and accurate diagnosis of vocal cord dysfunction, thereby preventing misdiagnosis and mistreatment as asthma. Future prospective validation studies will need to be performed. © **2013 American Academy of Allergy, Asthma & Immunology (J Allergy Clin Immunol Pract 2013;■:■-■)**

Key words: *Vocal cord dysfunction; Asthma; Clinical scoring index*

Vocal cord dysfunction (VCD), also known as paradoxical vocal fold motion disorder, is a common and often overlooked disorder characterized by abnormal adduction of the vocal cords, primarily during inspiration. Although the exact prevalence of VCD is not known, it has a higher incidence among women.[1,2] Symptoms of VCD, which include dyspnea, cough, dysphonia, and throat tightness, are often absent at rest but can sometimes be exacerbated by specific irritants.[3-5] The exact cause of VCD is unknown, although laryngeal hyperresponsiveness might be secondary to inflammation and/or irritation of the vocal cords. Gastroesophageal reflux disease, rhinitis with postnasal drip, viral upper respiratory tract infections, cold air, and chemical or occupational irritants have all been suggested to trigger VCD.[3-5] Psychosocial factors have been found to play a role in VCD as well.[6,7] The differential diagnosis for VCD is broad and includes anatomic defects of the upper airway, vagus or recurrent laryngeal nerves lesions, laryngeal edema, and uncontrolled asthma.[3-5] Proposed guidelines for the diagnosis of VCD include appropriate clinical history, evidence of abnormal vocal cord motion on laryngoscopy, and pulmonary function test criteria.[8] The management of VCD includes treatment directed at underlying comorbid conditions in addition to speech and behavioral therapy.[3]

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Abbreviations used
ANOVA- Analysis of variance
BMI- Body mass index
CI- Confidence interval
GERD- Gastroesophageal reflux
IBS- Irritable bowel syndrome
IQR- Interquartile range
N/A- Not available
NPV- Negative predictive value
OR- Odds ratio
PPV- Positive predictive value
SOB- Shortness of breath
VCD- Vocal cord dysfunction

Given its symptom overlap with asthma, VCD can remain misdiagnosed as asthma for a long period of time.[9,10] Our previous study found that 42.4% of patients with VCD were misdiagnosed with asthma for an average of 9 years.[11] Although both disorders can exist in isolation, there appears to be a population of patients in which both asthma and VCD coexist, although the nature of the relationship between the two has been debated.[12-14] Accurate and timely diagnosis of VCD has become ever more important, because a delay in diagnosis can result in increased asthma medication use and health care utilization.[11]

Although laryngoscopic examination remains the criterion standard for a diagnosis of VCD, the examination may be normal in between attacks if the appropriate trigger is absent. Conversely, abnormal vocal cord motion may be present during laryngoscopy in the absence of symptoms.[15] In addition, general practitioners are unlikely to perform laryngoscopy in the office setting, which necessitates referral to a specialist for diagnosis. In this study, we aimed to develop a simple, weighted scoring system based on patient symptoms and comorbidities to aid in the diagnosis of VCD in the clinical setting. This scoring system could be used to timely and accurately diagnose VCD, and it is hoped will result in decreased medication use and health care utilization in this population.

METHODS

Study design

We previously conducted a retrospective analysis of patients with isolated or coexisting VCD and asthma seen in an outpatient university asthma-allergy center.[11] In this study, we used the demographic, historical, and clinical information of subjects who were determined to have isolated VCD and isolated asthma. We specifically excluded any subjects with confirmed diagnoses of coexistent VCD and asthma to best differentiate between the 2 conditions. The diagnosis of VCD was based on the following diagnostic criteria: a consistent clinical history (prolonged symptoms, recurrent or intermittent episodes, reproducible inciting factors), symptoms (including dyspnea, upper airway stridor or wheezing, throat tightness, chest tightness, cough, or dysphonia), and positive findings on laryngoscopy.[8] Laryngoscopy was performed in all of the subjects by a single provider (A.A.P.), during which abnormal vocal cord motion or vocal cord collapse was noted. If no abnormal motion or collapse of the vocal cords was detected but the subject related a history of irritants, such as strong scents, odors, or exercise, that elicited his or her symptoms, a laryngoscopy was repeated with provocation (exercise challenge or exposure to a strong perfume), and the vocal cords were observed for abnormal motion and/or collapse. If there were no laryngoscopic findings of VCD, then these subjects were excluded from analysis. A total of 89 subjects with isolated VCD were included in this analysis.

TABLE I. Patient demographics

	VCD (n = 89)	Asthma (n = 59)	*P* value
Age (y), median (IQR)	47.0 (37.0-56.0)	38.0 (28.0-53.8)	.01*
BMI (kg/m^2), median (IQR)	29.0 (23.4-36.0)	26.9 (22.6-33.2)	.54
% Women (95% CI)	91.0 (83.3-95.4)	63 (53.2-71.8)	<.0001*
% Tobacco use (95% CI)	27.0 (18.8-37.0)	29 (21.0-38.5)	.26

BMI, Body mass index; *IQR,* Interquartile range.
*$P < .05$ was considered statistically significant.

For our asthma-alone group, 100 computer-generated randomly selected asthma patients (International Classification of Diseases, Ninth Revision, code of 493) were evaluated objectively for the presence of asthma. Fifty-nine subjects met criteria for an asthma diagnosis by using currently accepted criteria, including a consistent history, evidence of obstruction and bronchodilator response on spirometry, and/or positive bronchoprovocation challenge testing with methacholine, consistent with the 2007 National Asthma Education and Prevention Program Guidelines.[16]

Demographic and clinical data were obtained for all the subjects. Comorbidities were extracted from the patient's reported medical history. No attempt was made to prove or disprove any of the diagnoses examined, except for asthma and VCD, as described above. This study was approved by the institutional review board at our facility.

Statistical analysis

Statistical analysis was performed by using JMP software (SAS Institute Inc, Cary, NC). Pearson χ^2 tests compared categorical variables. For normally distributed data, ANOVA was used, whereas, for nonparametric numerical demographic data, the Kruskal-Wallis test was used to compare average ranks across groups; 95% CIs also were recorded.

To develop a scoring system, symptom and comorbidity variables to be included were guided by a review of the literature.[3-5,11] An unadjusted analysis was first performed to identify significant factors (with a liberal threshold of $P < .2$ for statistical significance) that might help distinguish VCD and asthma. Variables found to be significant in the unadjusted analysis were included in a multivariable logistic regression model. Those variables that were found to be independent predictors for the outcome ($P < .05$) were selected for the final model, and a stepwise backward elimination process used the likelihood ratio test to eliminate variables that did not significantly contribute to the model. Scores were assigned to each independent predictor found to be significant in the final model, with weights assigned according to the regression coefficients from the final model and rounding to the nearest integer. Receiver operating characteristic curves and the resulting area under the curve were also determined.

After determining the appropriate cutoff score, the scoring system was applied to an independent convenience sample, which consisted of an additional 72 subjects with VCD (confirmed on laryngoscopy) that were not included in our previous retrospective study nor used to develop the original scoring system. In *post hoc* analysis, the scoring system rule was

TABLE II. Analysis of demographics, comorbidities, symptoms, and triggers in the unadjusted and multivariable logistic regression model, and weights assigned in the final VCD score*

	VCD (n = 89)	Asthma (n = 59)	Crude OR	*P* value for crude OR	Adjusted OR	*P* value for adjusted OR	Score assigned
Patient characteristics							
No. of women/men	81/8	35/24	6.9 (2.9-17.9)	<.0001			
Age (y), median (IQR)	47 (37-56)	38 (29-53)	0.97 (0.95-1.0)	.02			
Height (cm), median (IQR)	163 (158-170)	168 (160-175)	1.05 (1.01-1.09)	.01			
No. of currently employed	57	40	2.1 (0.9-5.2)	.08			
Comorbidities, no. of patients							
Drug allergy	51	25	1.8 (0.9-3.6)	.07			
GERD	60	21	3.7 (1.9-7.6)	.002			
IBS	11	2	4.0 (1.0-26.6)	.045			
Psychiatric diagnosis	44	19	2.1 (1.0-4.1)	.04			
Chronic pain	22	9	1.8 (0.8-4.5)	.16			
Symptoms, no. of patients							
Cough	53	42	0.6 (0.3-1.1)	.11			
SOB	68	52	0.4 (0.2-1.1)	.07			
Heartburn	29	7	3.6 (1.5-9.5)	.003			
Dysphonia	**32**	**4**	**8.0 (2.9-28.2)**	**<.0001**	**5.1 (1.1-27.8)**	**.04**	**2**
Absence of wheezing	**60**	**12**	**8.1 (3.8-18.2)**	**<.0001**	**6.0 (1.9-21.0)**	**.002**	**2**
Throat tightness	**59**	**1**	**114.1 (23.3-2063.9)**	**<.0001**	**43.5 (7.3-847.8)**	**<.0001**	**4**
Triggers, no. of patients							
Stress	15	1	11.8 (2.3-215.6)	.001			
Exercise	26	32	0.4 (0.2-0.7)	.003			
Cold air	17	18	0.5 (0.2-1.2)	.11			
Odors	**62**	**5**	**24.8 (9.7-77.4)**	**<.0001**	**16.6 (4.8-68.9)**	**<.0001**	**3**

GERD, Gastroesophageal reflux disease; *IBS,* irritable bowel syndrome; *OR,* odds ratio; *SOB,* shortness of breath.
Note. Boldface indicates variables that were found to be significant.
*For all variables in the unadjusted analysis, the *P* value was < .2; only variables that remained after stepwise backward elimination (at *P* < .05) were included in the final model.

TABLE III. Performance characteristics of the Pittsburgh VCD Index at different cutoff points

Cutoff*	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)
11	0.15 (0.09-0.25)	1.0 (0.92-1.0)	1.0 (0.72-1.0)	0.44 (0.36-0.53)
9	0.47 (0.36-0.58)	1.0 (0.92-1.0)	1.0 (0.89-1.0)	0.56 (0.46-0.65)
8	0.50 (0.39-0.61)	1.0 (0.92-1.0)	1.0 (0.92-1.0)	0.57 (0.47-0.67)
7	0.58 (0.47-0.69)	1.0 (0.92-1.0)	1.0 (0.91-1.0)	0.62 (0.51-0.71)
6	0.67 (0.56-0.77)	0.98 (0.90-1.0)	0.98 (0.90-1.0)	0.67 (0.56-0.77)
5	0.78 (0.67-0.86)	0.97 (0.87-0.99)	0.97 (0.89-0.99)	0.74 (0.63-0.84)
4†	0.83 (0.73-0.90)	0.95 (0.85-0.99)	0.96 (0.88-0.99)	0.77 (0.67-0.87)
3	0.88 (0.77-0.94)	0.88 (0.76-0.85)	0.92 (0.83-0.96)	0.84 (0.71-0.91)
2	0.97 (0.89-0.99)	0.67 (0.54-0.79)	0.81 (0.72-0.88)	0.93 (0.79-0.98)
0	1.00 (0.95-1.0)	0 (0.0-0.08)	0.60 (0.51-0.68)	N/A

N/A, Not available; *NPV,* Negative predictive value; *PPV,* positive predictive value.
*A score of 1 or 10 is not possible when using the assigned values for each symptom or trigger.
†Optimal cutoff.

TABLE IV. Probability of VCD or asthma at various cutoff points

Cutoff*	Probability of VCD	Probability of asthma
0	0.08	0.92
2	0.34	0.66
3	0.57	0.43
4†	0.77	0.23
5	0.89	0.11
6	0.95	0.05
7	0.98	0.02
8	0.99	0.01
9	0.997	0.003
11	0.9995	0.0005

*A score of 1 or 10 is not possible when using the assigned values for each symptom or trigger.
†Optimal cutoff.

applied to the subjects with both VCD and asthma to test the performance of our scoring system in that population.

RESULTS

Study population for developing the scoring system

The study population consisted of 2 groups: (1) subjects with VCD alone (n = 89), and (2) asthma alone (n = 59). The subjects with VCD were significantly older than the subjects with asthma. There was no difference in body mass index or history of tobacco use among the groups (Table I). There were significantly more women in the VCD population, consistent with previous studies.[3]

Development of a scoring system

The results of the unadjusted analysis of the included demographics, comorbidities, symptoms, and triggers are summarized

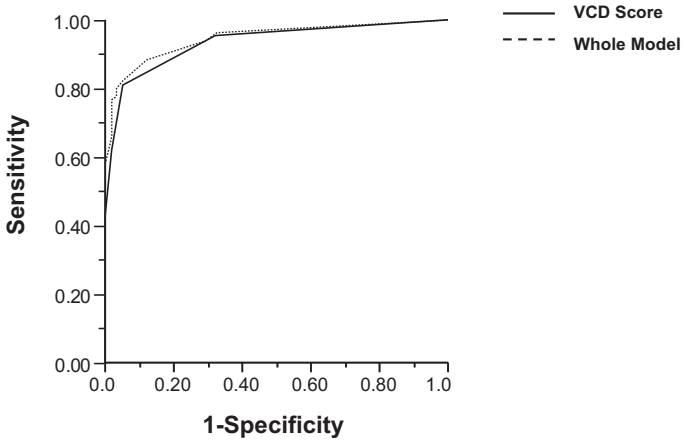

FIGURE 1. Receiver operating characteristic curves for the whole model and the Pittsburgh VCD Index.

TABLE V. Distribution of VCD scores in various study populations

VCD score*	VCD study subjects, no. (%) (n = 89)	Asthma study subjects, no. (%) (n = 59)	Convenience VCD subjects, no. (%) (n = 72)	Coexistent VCD and asthma subjects, no. (%) (n = 43)
0	4 (4.5)	40 (67.8)	2 (2.8)	4 (9.3)
2	8 (9.0)	12 (20.3)	12 (16.7)	6 (14.0)
3	5 (5.6)	4 (6.8)	2 (2.8)	3 (7.0)
4	4 (4.5)	1 (1.7)	6 (8.3)	3 (7.0)
5	9 (10.1)	1 (1.7)	4 (5.6)	4 (9.3)
6	8 (9.0)	1 (1.7)	10 (13.9)	1 (2.3)
7	8 (9.0)	0 (0)	8 (11.1)	8 (18.6)
8	3 (3.4)	0 (0)	3 (4.2)	2 (4.7)
9	27 (30.3)	0 (0)	20 (27.8)	7 (16.3)
11	13 (14.6)	0 (0)	5 (6.9)	5 (11.6)

*A score of 1 or 10 is not possible when using the assigned values for each symptom or trigger.

in Table II. After stepwise elimination, 4 variables were found to be significant and were retained for the final analysis. These variables were a patient-reported history of symptoms of throat tightness and dysphonia, the absence of wheezing, and the presence of odors as a symptom trigger. Based on the regression coefficients, weighted scores were assigned to these individual variables. The results of the multivariable analysis and scores assigned are summarized in Table II. Adjusting the final model for age did not affect the results ($P = .71$, likelihood ratio test).

The resulting scoring system for distinguishing VCD from asthma was tested at different cutoffs, with the results shown in Table III. A cutoff score of ≥ 4 gave a sensitivity of 83%, a specificity of 95%, a positive predictive value of 96%, and a negative predictive value of 77% and, given the balance of sensitivity and specificity, was determined to be the best cutoff for distinguishing VCD from asthma. By using prediction profiling, a cutoff score of ≥ 4 would give a 77% probability of having VCD. The probabilities of VCD at the various cutoff points are outlined in Table IV. Receiver operating characteristic curves for both the model and the scoring system are shown in Figure 1 (area under the curve = 0.9480 and 0.9350, respectively).

Application of the score

We tested the effectiveness of the scoring system by applying a cutoff score of ≥ 4 to a convenience population (n = 72). This was an additional population that had VCD proven on laryngoscopy but who had not been used in our previous retrospective study or in development of the scoring system. We thought that this was an ideal population in which to test our scoring system. By using our scoring system, 56 of 72 were correctly diagnosed with VCD (77.8%).

In addition, because subjects with both VCD and asthma can present a diagnostic dilemma, we sought to test our scoring system in a population previously demonstrated to have both conditions (n = 43).[11] In this population, our scoring system correctly identified 30 of 43 subjects as having VCD (69.8%). The distributions of scores for the various study populations are outlined in Table V. There was no statistically significant difference between the patient populations with VCD.

DISCUSSION

We developed the Pittsburgh VCD Index, a proposed simple scoring system that successfully distinguished VCD from asthma. Although many factors historically have been associated with VCD, such as comorbidities (gastroesophageal reflux disease, irritable bowel syndrome, psychiatric diagnosis, chronic pain), symptoms (heartburn, dysphonia, throat tightness), and triggers (stress, exercise, cold air, odors), our model indicates that symptoms of throat tightness and dysphonia, the absence of wheezing, and the presence of odors as a trigger for symptoms are most predictive of VCD.[3] By using the Pittsburgh VCD Index,

we found that a cutoff score of ≥4 had a high predictive value for the presence of VCD. We believe that this scoring system, with a few questions and no additional cost to the patient or medical practice, may aid general practitioners and specialists in distinguishing VCD from asthma. It may be especially useful in settings in which laryngoscopy is not available or not routinely performed. Moreover, when laryngoscopy is negative but clinical suspicion for VCD is high, it may be of use as well because laryngoscopy can be normal in between symptomatic episodes. In addition, we were able to apply our scoring system and demonstrate its applicability and reliability to another population with confirmed VCD and found that it correctly diagnosed VCD in 77.8% of subjects. Finally, the Pittsburgh VCD Index may help prevent misdiagnosis and mistreatment of VCD as asthma. In our previous study, we showed that subjects with VCD wrongly diagnosed as asthma generally had more asthma medication use and health care utilization, and remained misdiagnosed for an average of almost 9 years.[11]

Our proposed scoring index has limitations. The criterion standard for VCD diagnosis remains laryngoscopy, and our scoring system is not meant to replace laryngoscopy when clinically indicated. Although the primary purpose of the score is to help distinguish VCD from asthma and to prevent misdiagnosis (and, therefore, mistreatment), there is a population of subjects with VCD who have coexisting asthma. Although our scoring system identified 69.8% of subjects with coexistent VCD and asthma as having VCD, it is important to note that, if there is a strong clinical suspicion for asthma or if subjects are not improving with treatment for VCD alone, then further diagnostic tests (ie, spirometry or bronchoprovocation) should be performed. In fact, we similarly attempted to determine if there were any predictors that could distinguish subjects with coexistent VCD and asthma from those with VCD or asthma alone, but no predictors could be identified (data not shown). This stresses the need for further evaluation of possible asthma on an individual clinical basis.

In addition, our asthma-only population did not undergo laryngoscopy to rule out VCD, although the clinical history and available testing did not suggest that these subjects had VCD. It will be important for future prospective studies to address this by performing laryngoscopies in this population. Also, the subjects with VCD in this study were referred to an allergy/asthma clinic. Otolaryngologists often see this patient population as well, and it is possible that there are clinical differences between these patient populations, which will need to be further evaluated. Finally, many patients with VCD will have inspiratory stridor at times, which they identify as wheezing and which has traditionally been used in clinical definitions. In our scoring system, we have not tried to determine if the wheeze is originating in the upper or the lower airway, which may also be difficult to determine clinically. Although the absence of wheeze was noted in a large majority of our VCD population (60/89 subjects [67%]), 29 of 89 subjects with VCD (33%) did, in fact, report "wheeze." Conversely, only 12 of 59 subjects with asthma (20%) had an absence of wheeze. These data do not suggest that the presence of wheeze excludes the diagnosis of VCD; it is just more easily distinguished from asthma when that symptom is absent. In fact, with our scoring system, one can be diagnosed with VCD, even with wheezing, as long as either throat tightness or both dysphonia and sensitivity to odors are present. For our scoring system to be used in the diagnosis of VCD, all of the 4 indicated measures must be evaluated; the absence of wheeze is just one of these measures.

Although our scoring system performed well and had high negative predictive value, misclassification (false negatives) occurred in 22.8% of subjects in our convenience population with documented VCD. As with all diagnostic tests, this demonstrates that the test must be interpreted in the context of all available clinical information, and further testing and clinical follow-up should be ordered if necessary. In addition, the positive and negative predictive values must be interpreted with substantial caution because they are highly dependent on the prevalence of the outcome; other populations with a lower prevalence may show substantially worse results for the predictive values. The external validity of our scoring system will need to be further tested in other populations and ultimately in a prospective study.

The Pittsburgh VCD Index is the first scoring system developed for distinguishing VCD from asthma. If confirmed by prospective validation studies in a more broadly based population, it has the potential for materially enhancing our ability to distinguish between VCD and asthma. An earlier and more-accurate diagnosis could ultimately decrease health care utilization among subjects with VCD. It is simple to use and easily applied. If it is confirmed to have a high positive predictive value, it would be a valuable tool to diagnose VCD, but, if clinical suspicion of coexisting asthma is present, then further testing will still need to be performed.

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